Cardiovascular Risk and Known Coronary Artery Disease Are Associated With Colorectal Adenoma and Advanced Neoplasia

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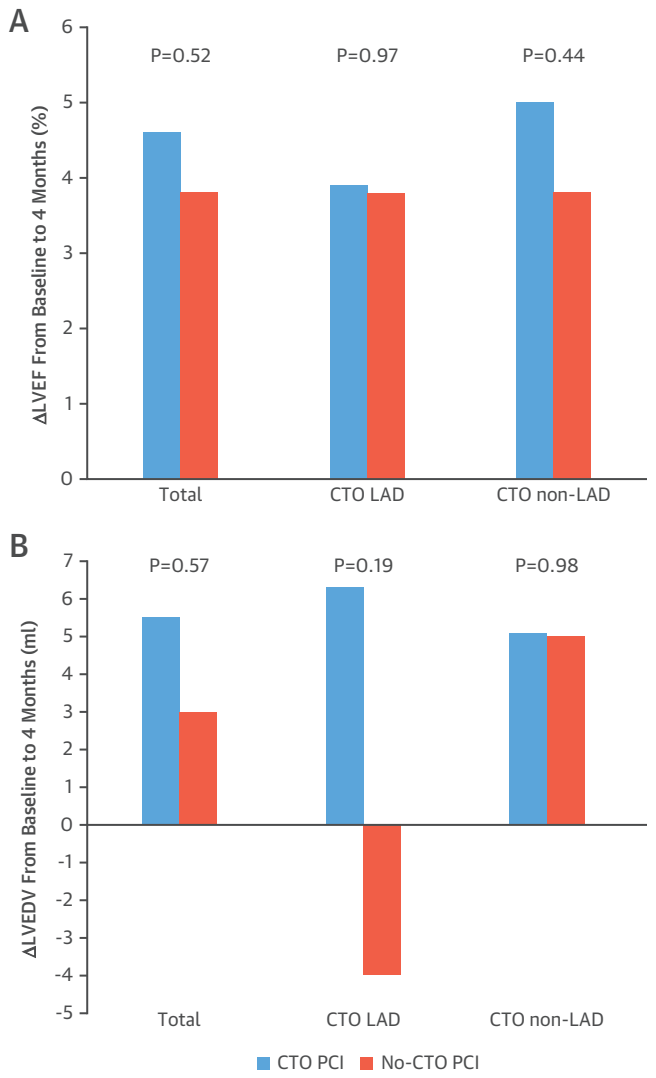
FIGURE 1 Recovery of LVEF and LVEDV in Total CMR Population and CTO LAD and CTO Non-LAD Patients, Comparing CTO PCI Versus No-CTO PCI



Delta **(A)** left ventricular ejection fraction (LVEF) and **(B)** left ventricular end-diastolic volume (LVEDV) between baseline and 4-month follow-up in total cardiac magnetic resonance imaging (CMR) population patients, chronic total occlusion (CTO) left anterior descending artery (LAD) and CTO non-LAD patients. Change in LVEF and LVEDV was compared between CTO percutaneous coronary intervention (PCI) **(blue)** and no-CTO PCI **(orange)**. Date are presented as means. Changes in LVEF and LVEDV were tested with independent samples *t* test.

reduced LVEF were mostly excluded. Furthermore, baseline LVEF was significantly different in the subgroups. All of these factors might have influenced the results.

In conclusion, the previous beneficial finding of CTO PCI in CTO LAD patients was not supported in serial CMR data. Therefore, the short-term results of the EXPLORE trial do not support a strategy of routine early CTO PCI in STEMI patients, regardless of CTO location. However, the effect of CTO PCI in more selected patients at a longer follow-up needs further evaluation.

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Cardiovascular Risk and Known Coronary Artery Disease Are Associated With Colorectal Adenoma and Advanced Neoplasia

Colorectal cancer is a potentially preventable disease, as early lesions may be detected and removed during screening colonoscopy. Emerging evidence suggests associations between cardiovascular disease and several cancers, including colorectal cancer. The relationship is thought to arise from common risk

factors including obesity, diabetes, hypertension, smoking, unhealthy diet, and physical inactivity (1).

We studied potential associations of cardiovascular risk (CVR), as assessed by the Framingham Risk Score (FRS) (2) or the presence of coronary artery disease (CAD), with colorectal neoplasia detected by screening colonoscopy in a Caucasian cohort without gastrointestinal symptoms.

The study was conducted in 2,098 participants of a health-screening program according to national screening recommendations for colorectal cancer between 2010 and 2014. All consecutive patients <79 years of age without gastrointestinal symptoms that asked to be screened and agreed to participate in the study were included. The study complies with the Declaration of Helsinki and was approved by the local ethics committee. Informed consent was obtained from all participants.

Colonoscopic findings were classified as tubular adenoma or advanced neoplasia (i.e., villous or tubulovillous features), size ≥1 cm or high-grade dysplasia, or carcinoma after analysis of macroscopic and histological results. Colonoscopic findings were defined as outcome variables, while all other variables as explanatory variables.

We used Statistica version 7.0 (StatSoft, Tulsa, Oklahoma) or Stata version 13.0 (Stata Corporation, College Station, Texas) statistical software. For comparison of categorical or continuous variables, we used a contingency chi-square test or analysis of variance, respectively. We estimated the odds ratio (OR) with 95% confidence interval (CI) by univariate logistic regression analysis. To provide separate ORs for the middle and upper FRS tertiles and the group with CAD history, we used 3 dummy variables with the low tertile as reference.

Clinical characteristics of our study population revealed associations of colonoscopic results with several CVR factors (**Table 1**). Our population included 108 (5%) subjects with a self-reported history of CAD. In 55 subjects, a previous coronary angiography verifying CAD was available. In the remaining 53 subjects, CAD history was verified by review of medical records. ORs for having any adenoma or advanced neoplasia in subjects with CAD history were 1.51 (95% CI: 1.10 to 2.27; p = 0.047) and 2.62 (95% CI: 1.31 to 5.20; p = 0.007), compared with subjects without CAD history, respectively.

Logistic regression models with FRS as predictor variable in subjects without CAD revealed that a 1-percentage-point increase of FRS was associated with ORs of 1.07 (95% CI: 1.06 to 1.09; p < 0.001) and 1.07 (95% CI: 1.04 to 1.12; p < 0.001) for the detection of any and advanced neoplasia, respectively.

TABLE 1 Characteristics of Subjects and Risk of Any Adenoma or Advanced Neoplasia by FRS Tertiles

	No Colorectal Adenoma (n = 1,534)	Any Colorectal Adenoma (n = 479)	Advanced Neoplasia (n = 85)	p Value
Age, yrs	58.0 ± 9.9	61.9 ± 8.8	63.8 ± 8.9	<0.001
Male	695 (45.3)	301 (62.8)	55 (64.7)	<0.001
Smoking status				0.292
Never	737 (48.0)	233 (48.6)	47 (55.3)	
Ever	558 (36.4)	170 (35.5)	21 (24.7)	
Current	239 (15.6)	76 (15.9)	17 (20.0)	
Arterial hypertension	942 (61.4)	317 (66.2)	53 (62.3)	0.170
Diabetes mellitus	199 (13.0)	81 (16.9)	17 (20.0)	0.028
FRS, %	6.9 ± 6.1	9.5 ± 6.5	10.8 ± 6.6	<0.001
HSESC, %*	2.8 ± 3.4	4.0 ± 3.6	5.4 ± 6.2	<0.001
History				0.010†
CAD	70 (4.6)	28 (5.8)	10 (11.8)	
MI	20 (1.3)	9 (1.9)	2 (2.4)	
Revascularization	36 (2.3)	18 (3.8)	7 (8.3)	

Risk of Any Adenoma or Advanced Neoplasia by FRS Tertiles

CVR/CAD Groups‡	Screened Subjects	Advanced Neoplasia
All subjects	2,098	85 (4.1)
Low FRS without CAD (0%–3%)	711	13 (1.8)
Intermediate FRS without CAD (4%–8%)	633	19 (3.0)
High FRS without CAD (>8%)	646	43 (6.7)
CAD	108	10 (9.6)

Values are mean ± SD, n (%), or n. Subjects with and without colorectal adenoma and advanced neoplasia differed significantly with respect to their (cardiovascular) characteristics. Risk of any adenoma or advanced neoplasia by FRS (estimates the 10-year risk of a subject to develop coronary heart disease) tertiles: number of screened subjects and the corresponding findings with respect to any colorectal adenoma or advanced neoplasia in low, intermediate, and high FRS and CAD groups. The p values refer to analysis of variance or contingency. Revascularization includes percutaneous stents and/or coronary artery bypass graft. *Estimates the 10-year risk of a subject for cardiovascular death. †Value for CAD history, not significant for MI/revascularization. ‡FRS upper limits of 3% and 8% for the low and intermediate risk groups were used, as other limits would have resulted in even greater deviations from equality among tertiles. Thus, 711, 633, and 646 subjects were assigned to the low, intermediate, and high tertiles. An additional analysis with an equal distribution of colorectal neoplasms among risk groups revealed essentially the same results.

CAD = coronary artery disease; FRS = Framingham Risk Score; HSESC = Heart Score of the European Society of Cardiology; MI = myocardial infarction.

In comparison to the low-risk FRS tertile (reference), the intermediate-risk (OR: 1.95; 95% CI: 1.49 to 2.55) and the high-risk tertiles (OR: 3.35; 95% CI: 2.59 to 4.33) showed stepwise increases in ORs for any colorectal adenoma (all p < 0.001) (**Table 1**). Additionally, for advanced neoplasia, a stepwise increase in ORs was observed as well: low-risk tertile (reference), intermediate-risk tertile (OR: 1.66; 95% CI: 0.81 to 3.39; p = 0.163), high-risk tertile (OR: 3.83; 95% CI: 2.04 to 7.19; p < 0.001), and CAD (OR: 5.47; 95% CI: 2.34 to 12.93; p < 0.001). Essentially, nearly identical results were observed when applying the Heart Score of the European Society of Cardiology (3) for the estimation of CVR (data not shown).

Our study has some limitations. CAD was established via questionnaire or medical history; however, neither coronary angiography nor other screening tests for CAD are justifiable in a population-based

screening study. Furthermore, FRS does not include diabetes, obesity, red meat or saturated fat intake, or family history of colorectal cancer, all of which are relevant for the assessment of colorectal cancer risk.

In conclusion, we report an association of CVR factors and colorectal neoplasms. In this screening cohort without gastrointestinal symptoms, subjects with known CAD and high CVR had a significantly higher probability of early and advanced colorectal neoplasia compared with subjects with low CVR, presumably due to shared risk factors. Our data suggest screening colonoscopy to be indicated particularly in subjects with known CAD or high CVR to detect potentially treatable colorectal neoplasia.

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The Influence of Exercise Therapy on the Heart Failure Disease Pathway

We would like to thank Kosmala et al. (1) for their recent publication, which expounded on the positive relationship between spironolactone and exercise tolerance in patients with heart failure (HF) with preserved ejection fraction. Their work has already garnered attention on the age-old adage of exercise and its relationship with disease management in HF. We would agree that exercise therapy could be a means of achieving quality of life endpoints as opposed to merely prolonging survival. Perhaps monitoring exercise tolerance along with standard biomarkers may reveal not only the progression of HF in individual patients, but also the effectiveness of exercise therapy over time.

As the management of HF is being relegated to the outpatient setting, it becomes increasingly clear that self-care is paramount in reducing readmissions and decreasing mortality rates in this population. Exercise therapy directly diminishes the levels of inflammatory biomarkers, such as tumor necrosis factor-alpha and interleukin, in the voluntary muscles of patients with HF (2). Because exercise augments cerebral perfusion (3) and directly counteracts the inflammatory response, exercise may be a cost-effective therapy in HF (4). If patients with HF were motivated to maximize self-care, a positive feedback loop could potentially arise where exercise improves executive function and affect to facilitate adherence to therapy and medication regimens.

Of course, it is not always that easy. In the United States alone, HF-associated costs will likely double from $31 billion to $70 billion from 2012 to 2030 (5). To add insult to injury, the aging population will in all probability increase the prevalence of and morbidity associated with HF management (5). HF has also been identified as a scourge on the international scale, discriminating not among nations of disparate resources. The onus of HF will in all likelihood continue to rise and is therefore a worldwide health concern that international bodies such as the World Health Organization are attempting to address (5).

This begs the question: Can the defeat of such a pernicious nemesis truly be carried out by exercise, which can be performed in one's own backyard? It is easy to say "yes." The true answer, however, lies in the will to act.

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